Background The 1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of SLE includes two autoantibody criteria: #10, abnormal level of anti-native DNA, anti-Sm, or antiphospholipid; #11 positive antinuclear antibody (ANA). Thus, ANA positivity is counted as 1 of the 11 criteria and a person shall be said to have SLE if any 4 or more of the 11 criteria are present, serially or simultaneously, during any interval of observation. The immunofluorescence pattern observed in the ANA test provides a direct initial assessment of ongoing autoantibody response in candidate patients of many systemic autoimmune rheumatic diseases (SARD). As a follow-up to the International Consensus on ANA Patterns (ICAP) initiative (ANAPatterns.org), which aims to promote harmonisation of ANA pattern nomenclature and provides guidelines for ANA interpretation, thereby optimising usage in patient care, the relevance of each ANA pattern is being re-evaluated.

Methods Collective issues on ANA nomenclature were raised among research, clinical, and diagnostic laboratories represented by two workshop participants and a working committee. Post-workshop exchanges arrived at consensus on a few, but clearly not all, issues. One focus is to establish an interpretative clinical description for each defined ANA pattern for clinical use based on current literature.

Results Consensus was achieved for 28 ICAP patterns designated with alpha-numeric code (AC-1 to AC-28) and summarised under a nomenclature and classification tree categorised in three major groups (nuclear, cytoplasmic, and mitotic patterns). An important observation is that, while the Homogeneous (AC-1) and Coarse Speckled nuclear (AC-5) patterns are linked to autoantibodies strongly associated with SARD, the Dense Fine Speckled (DFS) nuclear pattern (AC-2) virtually rules out a SARD diagnosis. A clear DFS pattern is usually present when anti-DFS70/LEDGF/P75 is the only predominant autoantibody in the serum sample. DFS is the most common pattern in high titer ANA-positive, apparently healthy, individuals. Although DFS has been reported in a wide variety of chronic inflammatory diseases, such as Hashimoto’s thyroiditis, atopic dermatitis, interstitial cystitis, Vogt-Koyanagi-Harada syndrome, and in miscellaneous non-inflammatory diseases, it is not associated with SARD, even when present at very high titer.

Conclusions ICAP has clearly provided a common platform to address issues that are of great interest to the ANA community and closely linked to ANA in disease criteria. Evidently, well-defined anti-DFS ANA, confirmed by antigen-specific reflex testing, should not be considered a criterion for SLE – either in the ACR or 2012 SLICC classification criteria.
Background T cell activation depends upon a calcium signalling cascade that is regulated by voltage-gated potassium channels. Effector memory T cells (TEM), which are implicated in the immunopathogenesis of autoimmune diseases, express relatively high levels of the potassium channel Kv1.3. Dalazatide is a potent peptide inhibitor of the Kv1.3 channel that has recently shown safety and efficacy in a Phase 1b plaque psoriasis trial. Evidence suggests that inflammatory cytokine producing TEM cells might be involved in the immunopathology of lupus nephritis. The objective of this study is to provide proof-of-principle ex vivo data for therapeutically targeting chronic T cell activation in systemic lupus erythematosus (SLE).

Materials and methods Peripheral blood mononuclear cells from paediatric and adult SLE patients as well as healthy controls were studied. T lymphocyte subsets were assayed ex vivo for Kv1.3 expression by flow cytometry. The effect of dalazatide on inflammatory cytokine expression by TEM cells activated by thapsigargin/phorbol myristate acetate (PMA) or ionomycin/PMA was evaluated by intracellular cytokine staining.

Results Kv1.3 expression by CD8+ TEM cells was significantly higher in patients with active lupus nephritis when compared to patients with inactive SLE or healthy controls. Dalazatide inhibited IFN-γ, IL-17 and TNF-α production by both CD4+ and CD8+ TEM cells from SLE patients in a dose-dependent manner. Dalazatide-mediated inhibition was more significant in IFN-γ and TNF-α-expressing CD4+ TEM cells from patients with active SLE compared to cells from patients with inactive disease.

Conclusions Ex vivo studies suggest that dalazatide inhibition of Kv1.3 on TEM may be an effective strategy for treating SLE. In addition, Kv1.3 expression may be a useful biomarker of SLE disease activity.

Background Patients with systemic autoimmune rheumatic diseases (SARD) often have a prolonged pre-clinical phase during which they are anti-nuclear antibody (ANA) but lack clinical symptoms. Here we sought to determine whether ANA+ individuals who lack sufficient symptoms for a SARD diagnosis share the B cell phenotypic changes seen in SARD.

Materials and methods Healthy controls (HC) and ANA+ individuals who: 1) lacked clinical symptoms of SARD (ANS); 2) had at least one clinical symptom of SARD (UCTD); or 3) had recently diagnosed steroid and immunosuppressive naïve SARD (SLE, SS, SSc, MCTD, DM) were recruited. PBMCs were stained with various combinations of fluorescently labelled antibodies and analysed by flow cytometry. Anti-nuclear antibodies were measured through the hospital laboratory. Whole blood IFN signature and BAFF RNA levels were measured by NanoString.

Results B cell phenotypes were examined for 32 HC, 38 ANS, 28 UCTD, and 59 early SARD patients. Patients with early SARD had a number of changes in their naïve and memory B cell subsets including: increased proportions of mature naïve (SSc and T1T2 cells (SLE and SjD), and decreased proportions of switched memory cells (all SARD). Similar decreases in the proportion of switched memory B cells were seen in ANS and UCTD patients, and as seen for the SARD patients, these cells were activated with elevated levels of CD86 as compared to HC. Significantly increased activation of the CD27+ IgD- memory compartment was also seen in ANS and UCTD patients. Nevertheless, in pre-SARD individuals, there was a trend to increased BAFF levels as compared to HC in pre-SARD individuals, which were not seen in ANS and UCTD patients. Although significantly increased proportions of plasmablasts and/or CD138+ plasma cells were seen in early SARD patients, these were not seen in ANS and UCTD patients. Nevertheless, in pre-SARD individuals (ANS + UCTD) there was a significant positive correlation between the size of these cell subsets and ANA titer as well as the number of different anti-nuclear antibody specificities. As observed for early SARD patients, there was a trend to increased BAFF levels as compared to HC in pre-SARD individuals, which achieved statistical significance in UCTD patients. However, there was no association between the levels of BAFF and any of the B cell phenotypes, whereas the IFN signature was positively associated with the proportion of T1T2 cells.